CLAIMS

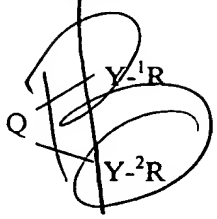
1. A chemical construct for use in solid phase synthesis comprising a solid support Q having linked thereto groups Y^1R and Y^2R; wherein R is a substrate or a coding tag and the groups Y^1 and Y^2 are connecting groups each having a first cleavage site, at least one of Y^1 and Y^2 having a second cleavage site located between the first cleavage site and group R, the first cleavage site being orthogonally and selectively cleavable with respect to the second cleavage site, and, when both groups Y^1 and Y^2 contain a second cleavage site, the second cleavage site in Y^1 being selectively and orthogonally cleavable with respect to the second cleavage site in Y^2; the second cleavage site being cleavable to release the substrate; and the first cleavage site being selectively cleavable to release a fragment Fr comprising the substrate R and at least a portion of the connecting group Y; and wherein:
(i) the chemical fragment Fr contains a sensitising group G which sensitises the chemical fragment Fr to instrumental, e.g. mass spectroscopic analysis and/or:
(ii) the fragment Fr contains a means for imparting a characteristic signature to the mass spectrum of the fragment.

2. A chemical construct according to claim 1 wherein at least one group R is a substrate.

3. A chemical construct according to claim 2 wherein the substrate is a drug molecule.

4. A chemical construct according to claim 1 comprising a solid support Q having linked thereto groups Y^1R and Y^2R, wherein R is a substrate (such as a drug molecule) and the groups Y^1 and Y^2 are connecting groups each having first and second cleavage sites which are orthogonally and selectively cleavable, the second cleavage site in Y^1 being selectively and orthogonally cleavable with respect to the second cleavage site in Y^2; the second cleavage site being cleavable to release the substrate; and the first cleavage site being located at a position between the second cleavage site and the solid support and being selectively cleavable to release a fragment Fr comprising the substrate R and at least a portion of the connecting group Y; and wherein:
(i) the chemical fragment Fr contains a sensitising group G which sensitises the chemical fragment Fr to instrumental, e.g. mass spectroscopic analysis and/or:
(ii) the fragment Fr contains a means for imparting a characteristic signature to the mass spectrum of the fragment.

5. A chemical construct according to claim 1 having the formula:



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6. A chemical construct according to any one of the preceding claims wherein each solid support contains a coding tag or coding sequence which encodes information indicative of at least part of the synthesis history of the construct.

7. A chemical construct according to claim 6 wherein the coding tag is a coding sequence linked to the solid support.

8. A chemical construct according to claim 7 wherein the coding sequence is linked to the solid support by means of a connecting group Y^a having a cleavage site cleavable to release a fragment F^a from the solid support, the fragment F^a comprising the coding sequence and optionally at least a portion of the connecting group Y^a.

9. A chemical construct according to claim 8 wherein:
(i) the chemical fragment F^a contains a sensitising group G which sensitises the chemical fragment F^a to instrumental, e.g. mass spectroscopic analysis and/or:
(ii) the fragment F^a contains a means for imparting a characteristic signature to the mass spectrum of the fragment.

10. A chemical construct according to claim 8 wherein the cleavage site of group Y^a is cleavable under conditions corresponding to those needed to cleave the first cleavage sites in the groups Y^1R and Y^2R.

11. A chemical construct according to claim 9 wherein the chemical fragment F^a contains a sensitising group G which sensitises the chemical fragment F^a to instrumental, e.g. mass spectroscopic analysis.

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12. A chemical construct according to any one of the preceding claims wherein a proportion of the total substrate R in the construct is linked to the solid support by means of a connecting group Y^b having a cleavage site which is cleavable to release a fragment F^b

from the solid support, the fragment F^b comprising the substrate R and at least a portion of the connecting group Y^b; the connecting group Y^b not being cleavable to release substrate R under conditions effective to cleave the second cleavage sites in the groups Y^1R and Y^2R and wherein:

(i) the chemical fragment F^b contains a sensitising group G which sensitises the chemical fragment F^b to instrumental, e.g. mass spectroscopic analysis and/or:

(ii) the fragment F^b contains a means for imparting a characteristic signature to the mass spectrum of the fragment.

13. A chemical construct according to any one of the preceding claims wherein the sensitising group G is generated by cleavage at the first cleavage site of the group Y^1 or Y^2 or, when present, Y^a or the said cleavage site of Y^b.

14. A chemical construct according to any one of the preceding claims wherein the sensitising group G is a basic amino group or a carboxylate group, preferably a basic amino group.

15. A chemical construct according to claim 14 wherein the sensitising group is a primary amino group, a secondary amino group, or a tertiary amino group.

16. A chemical construct according to claim 15 wherein the sensitising group is a tertiary amino group selected from cyclic amino groups such as piperidino, piperazino (e.g.N-methylpiperazino), pyrrolidino, or morpholino, piperidino.

17. A construct according to any one of the preceding claims wherein the fragment Fr and (where present) optionally the fragment F^a and (where present) optionally the fragment F^a contain a means for imparting a characteristic signature to the mass spectrum of the fragment.

18. A construct according to claim 17 wherein the signature is provided by incorporating into the fragment a "peak splitting" isotopic label comprising at least one atom that exists in a number of stable isotopic forms.

19. A chemical construct according to claim 18 wherein the fragments Fr and F^a, and (where present) optionally F^c are labelled differently so as to produce different characteristic

signatures.

20. A chemical construct according to claim 18 or claim 19 wherein the isotopic label comprises an atom or atoms selected from $^{1}H/H^{2}$ (D), $^{79}Br/^{81}Br$, $^{12}C/^{13}C$, $^{14}N/^{15}N$ and $^{16}O/^{18}O$.

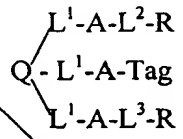
21. A chemical construct according to any one of claims 18 to 20 wherein the isotopic label(s) is/are located between the first and second cleavage sites of the groups Y^1 and Y^2.

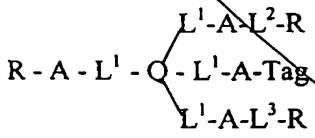
22. A chemical construct as defined in any one of the preceding claims wherein the first and second cleavage sites in the groups Y^1 are defined by first and second linker groups L^1 and L^2, first and second cleavage sites in the group Y^2 are defined by first and second linker groups L^1 and L^3, the cleavage site in the group Y^a (where present) is defined by a linker group L^a and the cleavage site in the group Y^b (where present) is defined by a linker group L^b.

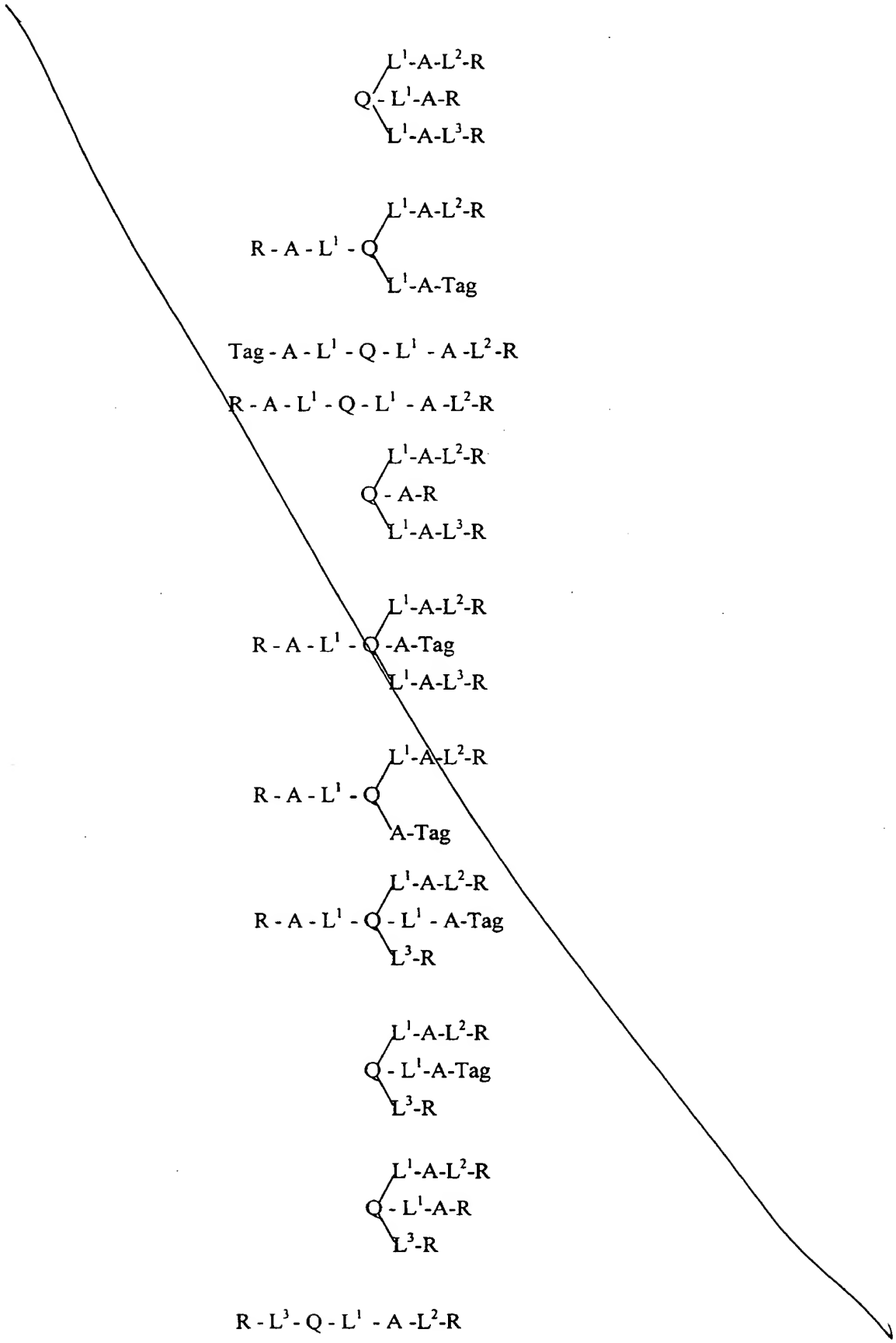
23. A chemical construct according to claim 22 wherein the linker groups L^a and L^b correspond to L^1.

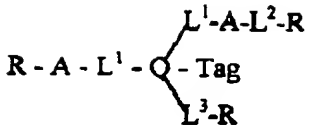
24. A chemical construct according to claim 22 or claim 23 wherein a spacer group A is interposed between each pair of first and second linker groups, or between the linker group L^a and the coding tag, or between the linker group L^b and the substrate R, the spacer group A containing an isotopic peak splitting label.

25. A chemical construct according to any one of the preceding claims having a formula selected from the group consisting of:






L1-A-L2-R
Q - L1-A-R
L1-A-L3-R
L1-A-L2-R
R - A - L1 - Q
L1-A-Tag
Tag - A - L1 - Q - L1 - A -L2 -R
R - A - L1 - Q - L1 - A -L2-R
L1-A-L2-R
Q - A-R
L1-A-L3-R
L1-A-L2-R
R - A - L1 - Q -A-Tag
L1-A-L3-R
L1-A-L2-R
R - A - L1 - Q
A-Tag
L1-A-L2-R
R - A - L1 - Q - L1 - A-Tag
L3-R
L1-A-L2-R
Q - L1-A-Tag
L3-R
L1-A-L2-R
Q - L1-A-R
L3-R
R - L3 - Q - L1 - A -L2-R



wherein L^1, L^2, L^3, A and R are as defined in any one of the preceding claims and "Tag" represents a coding sequence.

26. A construct as claimed in any one of claims 1 to 25 for use in a tiered release method of screening, the construct having the formula Tag - A - L^1 - Q - L^1 - A -L^2 - R wherein Tag, A, L^1, Q ,L^2 and R are as defined in any one of the preceding claims.

27. A chemical construct according to any one of the preceding claims wherein the orthogonally cleavable cleavage sites can be cleaved by a reactions selected from acid catalysed cleavage, base catalysed cleavage, oxidative cleavage, reductive cleavage, nucleophilic displacement, electrophilic displacement, and thermal, photochemical and enzymatic cleavage.

28. Intermediate chemical constructs for use preparing a chemical construct as defined in any one of the preceding claims, the intermediate constructs having the formulae $Y^{1'}$-Q-$Y^{2'}$, RY^1-Q-$Y^{2'}$and $Y^{1'}$-Q-Y^2R wherein $Y^{1'}$ and $Y^{2'}$ are reactive or protected forms of the group Y; and R, Q and Y are as defined in any one of the preceding claims.

29. Intermediate constructs of the formulae $L^{2'}$-A-L^1-Q-L^1-A^P, R-L^2-A-L^1-Q-L^1-A^P, $L^{3'}$-A-L^1-Q-L^1-A^P, R-L^3-A-L^1-Q-L^1-A^P, R-L^3-A-L^1-Q-L^1-A-$L^{2'}$ and $L^{3'}$-A-L^1-Q-L^1-A-L^2-R wherein $L^{1'}$, $L^{2'}$ and $L^{3'}$ are reactive or protected forms of the linker groups L^1, L^2 and L^3, A^P is a reactive or protected form of the spacer group A containing a peak splitting isotopic label, and Q, R, A, L^1, L^2 and L^3 are as defined in any one of the preceding claims.

30. An intermediate construct according to claim 29 wherein the group A^P has the formula NH-Alk-NX^1 wherein Alk is an alkylene group and X^1 is hydrogen or an aralkyl group.

31. An intermediate construct according to claim 29 or claim 30 wherein the solid support has bonded thereto a coding tag sequence L^1-A-Tag and/or a sequence R - A - L^1 -, or a precursor form thereof..

32. A differential release method of assaying a chemical library for bi logical activity, the method comprising:

(i) subjecting a construct comprising a solid support Q having linked thereto groups Y^1R and Y^2R as defined in any one of the preceding claims to cleavage conditions effective to release substrate R from the group Y^1R;

(ii) testing the substrate R released from the group Y^1R in a biological assay;

(iii) subsequently subjecting the construct to cleavage conditions effective to release substrate R from the group Y^2R; and

(iv)) testing the substrate R released from the group Y^2R in a biological assay.

33. A tiered release method of assaying a chemical library for biological activity, the method comprising:

(i) subjecting a construct as claimed in any one of claims 1 to 27 to cleavage conditions effective to release a first portion of the substrate R from the group Y^1R;

(ii) testing the first portion of substrate R released from the group Y^1R in a biological assay;

(iii) subjecting the construct to cleavage conditions effective to release a second portion of the substrate R from the group Y^1R; and

(iv) testing the second portion of substrate R released from the group Y^1R in a biological assay.

34. A method of determining the identity of a substrate R linked to a solid support Q of a construct as claimed in any one of claims 8 to 27 by mass spectrometric means; the solid support Q having a coding sequence attached thereto by means of a connecting group Y^a having a cleavage site cleavable to release a fragment F^a from the solid support, the fragment F^a comprising the coding sequence and at least a portion of the connecting group Y^a, wherein (i) the chemical fragment F^a contains a sensitising group G which sensitises the chemical fragment F^a to mass spectroscopic analysis;

the coding sequence comprising a sequence of coding groups the nature and order of which is indicative of the identity of the substrate R;

the method comprising cleaving the connecting group Y^a so as to release the fragment F^n from the solid support; subjecting the fragment Y^a to mass spectrometry under conditions effective to bring about mass spectral fragmentation of the coding group and the formation of mass spectral fragment ions corresponding to the loss of one or more coding groups from the coding sequence, and thereafter correlating mass

spectral peaks of the mass spectral fragment ions with the molecular ion of the fragment Y^a to identify the sequence of the individual coding groups.

35. A method according to claim 34 wherein the fragment F^a contains a means for imparting a characteristic signature to the mass spectrum of the fragment.

36. A method of identifying a pharmaceutically useful substrate comprising preparing a library containing a plurality of chemical constructs as defined in any of the preceding claims, and subjecting the library to biological testing to identify biologically active substrates.

37. A method according to claim 36 that includes the further step of formulating a biologically active substrate thus identified with a pharmaceutically acceptable carrier to form a pharmaceutical composition.